**UNITED STATES PATENT AND TRADEMARK OFFICE**

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

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*Ex parte* DANIEL ALBERT and DANIEL CIMBORA

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Appeal 2007-1612
Application 10/099,924
Technology Center 1600

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Decided: August 23, 2007

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Before ERIC GRIMES, DEMETRA J. MILLS, and NANCY J. LINCK, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a protein complex. The Examiner has rejected the claims as including new matter, lacking an adequate description in the Specification, and nonenabled. We have jurisdiction under 35 U.S.C. § 6(b). We affirm the written description rejection, affirm-in-part the new matter rejection, and reverse the enablement rejection.

## BACKGROUND

"Survivin is one of the few known proteins that integrate cell cycle progression and programmed cell death" (Specification 22). "It has been discovered that survivin specifically interacts with cytoplasmic dynein light chain 1 ('HDLC1')," among other proteins (Specification 6). "The specific interactions between these proteins and survivin suggest that survivin and the survivin-interacting proteins are involved in common biological processes. . . . For example, they may be involved in apoptosis. Thus, the survivin-interacting proteins and the protein complexes are potential drug targets." (*Id.*)

## DISCUSSION

1. CLAIMS

Claims 40-50 are on appeal. Claims 11-26 are also pending but have been withdrawn from consideration by the Examiner.

The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claim 40 is representative and reads as follows:

Claim 40. An isolated protein complex comprising a first protein interacting with a second protein, wherein said first protein is selected from the group consisting of:

(a) survivin, or a fragment thereof that interacts with HDLC 1;

(b) a first polypeptide having an amino acid sequence at least 80% identical to that of (a), and that interacts with HDLC 1; and

(c) a first fusion protein comprising (a) or (b); and

wherein said second protein is selected from the group consisting of:

(i) HDLC 1, or a fragment thereof that interacts with survivin;

(ii) a second polypeptide having an amino acid sequence at least 80% identical to that of (i), and that interacts with survivin; and

(iii) a second fusion protein comprising (i) or (ii).

2. PRIOR ART

The Examiner relies on the following references:

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|---|---|---|
| Snyder | US 6,168,926 B1 | Jan. 2, 2001 |
| Altieri | US 6,800,737 B2 | Oct. 5, 2004 |

3. NEW MATTER

Claims 40-50 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that certain claim limitations are not adequately supported in the Specification and therefore constitute new matter. The Examiner states:

> The specification seems to be remiss of amino acid residues 47 to 99 of survivin interacting with HDLC1, fragment thereof, or a polypeptide 80% or 90% identical to HDLCI. Likewise, it is unclear where in the specification Appellant have contemplated only 80%, 90% or a contiguous span of 10 amino acids of a first polypeptide, survivin interacting with at least 80%, 90% or a contiguous span of 10 amino acids of a second polypeptide.

(Answer 4.)

As we understand it, the Examiner's position is that the following limitations are new matter: (1) a fragment of survivin comprising amino acids 47 to 99 that interacts with HDLC1; (2) polypeptides that are at least 80% or 90% identical to survivin that interact with HDLC1; (3) polypeptides comprising 10 contiguous amino acids of survivin that interact with HDLC1; (4) polypeptides that are at least 80% or 90% identical to HDLC1 that interact with survivin; and (5) polypeptides comprising 10 contiguous amino acids of HDLC1 that interact with survivin.

Appellants point to specific disclosures in the Specification as supporting the challenged claim limitations (Br. 6).

We agree with Appellants that the "80% identical," "90% identical," and "10 contiguous amino acids" limitations are adequately disclosed in the Specification as filed. The Specification states that

> the term "homologue" . . . means a polypeptide that exhibits an amino acid sequence homology and/or structural resemblance . . . such that it is capable of interacting with the second native protein. Typically, a protein homologue of a native protein may have an amino acid sequence that is at least 50%, . . . more preferably at least 80%, . . . even more preferably at least 90% . . . identical to the native protein.

(Spec. 17: 6-14.)

The Specification also states that

> potentially useful agents also include incomplete proteins, i.e., fragments of the interacting protein members that are capable of binding to their respective binding partners in a protein complex. . . . For example, suitable protein fragments can include polypeptides having a contiguous span of . . . 10 . . . amino acids or more of the sequence of survivin that are capable of interacting with . . . HDLC1. . . . Alternatively, a polypeptide capable of interacting with survivin and having a contiguous span of . . . 10 . . . amino acids of . . . HDLC1 . . . may be administered.

(*Id.* at 96: 15 to 97: 11.)

These disclosures adequately describe the "80% identical," "90% identical," and "10 contiguous amino acid" claim limitations. While the Examiner may be correct that the Specification does not expressly describe 80% or 90% identical fragments of survivin or HDLC1 that interact with each other, a claim limitation need not be described in the same words in order to be adequately described. *See Purdue Pharma v. Faulding, Inc.*,

230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue."). In our view, the Specification describes these claim limitations adequately to satisfy 35 U.S.C. § 112, first paragraph.

However, we agree with the Examiner that the claims language reciting amino acids 47 to 99 of survivin lacks adequate support in the Specification and therefore constitutes new matter. Appellants point to the Specification's Table 1, which discloses that the following fragments of survivin interact with HDLC1: amino acids 89 to 143, amino acids 3 to 99, and amino acids 47 to 99 (Specification 21). Appellants argue that

> [a]nyone skilled in the art would immediately recognize from this that the interaction domain of survivin (responsible for the interaction with HDLC 1) is probably within amino acid residues 47 - 99. Thus, by showing the overlap between these fragments and claiming fragments comprising this overlapping region, Appellants have fully described and supported this limitation.

(Reply. Br. 6.)

Appellants' argument is not supported by the evidence in the record. The Specification interprets the data in Table 1 as follows:

> Searches of the brain library with survivin (aa 3-99 and 47-142) also identified cytoplasmic dynein light chain 1 (HDLC1) as an interactor. . . . Survivin is 142 amino acids long, and the previous survivin bait that isolated HDLC1 is amino acids 89-142. *HDLC1 either interacts with both the N-terminus (aa 3-99) and C-terminus (aa 89-142) of survivin, or we have fortuitously identified a core HDLC1 binding site on survivin, namely aa 89-99.*

(Spec. 23: 25-31, emphasis added.)

Thus, when the inventors themselves interpreted the data in Table 1, they concluded that either (1) survivin has two interaction domains, one each in the N- and C-terminus, or (2) survivin's interaction domain is in amino acids 89 to 99. The inventors themselves did not attach any significance to the part of survivin from *amino acid 47* to amino acid 99, belying Appellants' assertion that "[a]nyone skilled in the art would immediately recognize" the importance of that fragment of survivin.

The Specification does not adequately describe the fragment of survivin comprising amino acids 47 to 99. We therefore affirm the rejection of claims 43, 49, and 50 as encompassing new matter. However, the Specification adequately describes the other claim limitations challenged by the Examiner, so we reverse the new matter rejection of claims 40-42 and 44-48.

4. ENABLEMENT

Claims 40-50 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that the experimentation required to make and use variants of survivin and HDLC1 would be "unnecessarily and improperly extensive and undue" (Answer 10). The Examiner acknowledges that survivin and HDLC1 are known in the art and that "one of ordinary skill in the art can theoretically produce all of these proteins with art known techniques" (*id.* at 8), but concludes that undue experimentation would be required because the effect of amino acid changes on protein function are unpredictable and the Specification provides little guidance regarding which positions in survivin and HDLC1 are tolerant of modification (*id.* at 9-10).

Appellants argue that

> [b]ecause the experimentation needed to practice the claimed invention is routine and not undue, Appellants respectfully assert that Examiner has failed to establish a prima facie case of nonenablement. In order to produce one protein complex in accordance with the present invention, an artisan need simply produce a survivin and/or HDLC 1 variant and test its ability to interact with a corresponding variant.

(Br. 14.) Appellants argue that the Specification provides sufficient guidance to enable those skilled in the art to make and test variants of survivin and HDLC1:

> Creating variants of a well-known peptide is routine to the point of bordering on the mundane. See generally Specification, p. 30-35 (describing several art-known techniques and citing to several art sources). Testing for a protein interaction between two known peptides is similarly unremarkable. Specification, p. 42-50.

(*Id.* at 15.) Thus, Appellants conclude, undue experimentation would not be required to make and use the full scope of the claimed complexes (*id.*).

We agree with Appellants that the Examiner has not adequately established that practicing the full scope of the claims would require undue experimentation. "[T]he question of undue experimentation is a matter of degree. . . . The Patent and Trademark Office Board of Appeals summarized the point well when it stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

*PPG Indus. v. Guardian Indus.*, 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996) (quoting *Ex parte Jackson*, 217 USPQ 804, 807 (1982)).

Here, the Examiner has acknowledged that those of skill in the art can make variants of survivin and HDLC1 "with art known techniques" (Answer 8). And, as Appellants point out, the Specification discloses that "homologues and derivatives . . . can be tested to determine whether they are capable of interacting with their intended partners to form protein complexes. Testing can be conducted by e.g., the yeast two-hybrid system or other methods known in the art for detecting protein-protein interaction" (Spec. 35: 1-4; see also *id.* at 57-73 (describing two-hybrid assays)).

Thus, the evidence of record shows that no more than routine experimentation would be required to make and test the survivin and HDLC1 variants encompassed by the claims. Certainly, the amount of experimentation required would be large. However, in view of the state of the art and the level of skill of those in the art, the Examiner has not adequately explained why the experimentation would have be "unduly extensive." *Atlas Powder Co. v. E.I. DuPont De Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). The rejection for nonenablement is reversed.

5. WRITTEN DESCRIPTION

Claims 40-50 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of an adequate written description. The Examiner reasons that, although the Specification discloses that full-length HDLC1 binds to three specific fragments of survivin (Answer 5), "[t]here is no description of the sites at which variability may be tolerated. Structural features that could

distinguish the compounds in the genus from others excluded are missing from the disclosure. . . . Information regarding how to make a variant or an assay for detecting the activity of a variant is not a showing of possession of the entire genus claimed." (*Id.* at 7.)

As we understand it, the Examiner's reasoning is that the claims encompass two genera of proteins; specifically, proteins that vary in as much as 20% of their amino acid sequence compared to survivin or HDLC1 but that still interact with HDLC1 or survivin. The Specification, however, does not disclose the structural features of survivin or HDLC1 responsible for the interaction of the two proteins, and therefore the Specification does not show that Appellant was in possession of the genera of 80% identical, interacting proteins encompassed by the claims.

We agree with the Examiner's reasoning and therefore affirm the rejection. To describe a genus of functional variants, a specification must provide guidance regarding which variants within the genus have the recited function.

On facts similar to those here, the U.S. Court of Appeals for the Federal Circuit has held claims to lack adequate description. In *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), the court held that claims generically reciting cDNA encoding vertebrate or mammalian insulin were not adequately described by the disclosure of cDNA encoding rat insulin. *Id.* at 1568, 43 USPQ2d at 1406. The court held that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish

> the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

*Id.* The court held that a

> description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

*Id.* The court has since clarified that the complete structure of the representative species does not necessarily have to be described. *See Enzo Biochem v. Gen-Probe*, 323 F.3d 956, 964-65, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002).

*Eli Lilly* supports our conclusion that the instant specification does not adequately describe the recited genera of proteins. The *Eli Lilly* court held that a fully described genus is one for which a person skilled in the art can "visualize or recognize the identity of the members of the genus." Here, as the examiner has pointed out, the specification provides does not provide guidance regarding what structural features are responsible for survivin/HDLC1 interaction, nor does it describe what amino acid changes can be made in the wild-type sequences without affecting the interaction of the proteins.

Thus, the Specification does not describe the recited genera sufficiently to allow a person skilled in the art to determine whether a given

80% identical HDLC1 or survivin variant is within the scope of the instant claims. Since the Specification does not describe the recited genera adequately for those skilled in the art to distinguish the HDLC1 and survivin variants within the claims from other HDLC1 or survivin variants, the Specification does not adequately describe the recited genera under the standard of *Eli Lilly*.

The court also confronted similar facts in *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 69 USPQ2d 1886 (Fed. Cir. 2004). In that case, the patent claimed a method of selectively inhibiting the enzyme PGHS-2 (also known as COX-2) by "administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product to a human." *Id.* at 917, 69 USPQ2d at 1888. The patent "described in detail how to make cells that express either COX-1 or COX-2, but not both . . . , as well as 'assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product.[']" *Id.* at 927, 69 USPQ2d at 1895.

The court held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of *which* peptides, polynucleotides, or small organic molecules have the desired characteristic, the claims were not adequately described. *See id.* ("As pointed out by the district court, the '850 patent does not disclose just 'which "peptides, polynucleotides, and small organic molecules" have the desired characteristic of selectively inhibiting

PGHS-2.' . . . Without such disclosure, the claimed methods cannot be said to have been described.").

Just as in *University of Rochester*, the present application discloses a genus of chemical compounds (proteins having amino acid sequences at least 80% identical to HDLC1 or survivin) but the claims are limited to only those compounds having a desired characteristic (interacting with the other protein). Just as in *University of Rochester*, the present specification does not disclose which of the many amino acid sequences that are at least 80% identical to survivin or HDLC1 have the recited interacting properties.

Granted, those skilled in the art could screen libraries of survivin and HDLC1 variants to identify for themselves specific proteins that are at least 80% identical to the wild-type sequence and that have the same interacting property. That, however, does not make up for the deficiency of the Specification's description. The *University of Rochester* court specifically noted that the patent at issue there disclosed screening assays to identify compounds having the desired characteristic, but nonetheless held that the description was inadequate. The same holds true here.

Appellants argue that the instant claims are adequately described under the standard applied in *Invitrogen Corp. v. Clontech Labs.*, 429 F.3d 1052, 77 USPQ2d 1161 (Fed. Cir. 2005) (Br. 7-9). Appellants argue that the claims in *Invitrogen* were directed to a modified reverse transcriptase (RT) protein – one having DNA polymerase but not RNase H activity – while the instant claims are directed to a complex comprising modified survivin and/or HDLC1 proteins:

> Like the claims in *Invitrogen*, Appellants' claims are also defined by polypeptides (survivin, HDLC 1 and fragments and

> specific homologs thereof) with specific functional limitations (capability of specific protein interactions). The instant Specification clearly provides support for such claims by describing (1) structure in the form of the amino acid sequence of representative embodiments of the claimed interacting proteins and fragments thereof; and (2) function in the form of a specific interaction between the first and second protein or fragments thereof. See Specification, p. 21, Table 1.

(Br. 8.) Appellants conclude that, "under *Invitrogen*, there is a sufficient written description in the Specification for the modified protein complexes" (*id.* at 9).

In our view, *Invitrogen* is distinguishable on its facts. The district court in that case relied on the specifications of the patents in suit (including U.S. Patent 5,244,797), testimony from Invitrogen's expert, and a prior art research paper[1] and determined that the evidence showed "a sufficiently known correlation between RNase H activity in RT (function) and the RT gene made by deletion mutation (structure) to satisfy" the test for written description set out in the USPTO Written Description Examination Guidelines. *Invitrogen*, 429 F.3d at 1072, 77 USPQ2d at 1175.

More specifically, the evidence in *Invitrogen* showed that

> [c]omputer analysis of the amino acid sequences from the putative gene products of retroviral pol genes has revealed a 150-residue segment at the carboxyl terminus that is homologous with the ribonuclease H of *E. coli* and a section close to the amino terminus which can be aligned with nonretroviral polymerases

('797 patent, col. 2, ll. 21-26, citing Johnson, *supra* note 1.)

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[1] Johnson et al., "Computer analysis of retroviral *pol* genes: Assignment of enzymatic functions to specific sequences and homologies with nonviral enzymes," *Proc. Natl. Acad. Sci. USA*, Vol. 83, pp. 7648-7652 (1986).

> The evidence also showed that, by making various deletions,
>
> the regions within the RT molecule responsible for DNA polymerase and RNase H activity have been identified. DNA polymerase was mapped to the amino half of the molecule, and RNase H to within 200 amino acids of the carboxy end, confirming the predictions based upon amino acid homology (Johnson, M.S. et al., supra). . . .
>
> . . . The results presented here show that of the 684 amino acids in pRT601 RT, residues between amino acid 212 and 314 are required for DNA polymerase activity, and residues between amino acid 503 and 611 are required for RNase H activity.

('797 patent, col. 17, ll. 13-51.)

Thus, the evidence in *Invitrogen* showed that those skilled in the art knew which domains of reverse transcriptase were necessary for the polymerase and RNase H activities and that at least one reverse transcriptase variant had been made that had the properties recited in the claims – having DNA polymerase activity but not RNase H activity.

In this case, by contrast, the evidence shows only that full-length HDLC1 interacts with amino acids 89-143, 47-143, or 3-99 of survivin. The Specification discloses no variants that change any of the naturally occurring amino acids of survivin or HDLC1. Appellants have pointed to nothing in the Specification or known in the art that would direct those skilled in the art to the part(s) of HDLC1 responsible for survivin interaction, or to specific amino acids in either survivin or HDLC1 that mediate interaction with the other protein. Thus, the evidence of record here does not provide the correlation between structure and function that the district court found to be known in *Invitrogen*.

Appellants also argue that the adequacy of the Specification's written description is supported by the USPTO Written Description Examination Guidelines and particularly by Example 14 of the Training Materials accompanying those Guidelines (Br. 9-12). We disagree. Appellants argue that the Specification shows possession of the "necessary common attributes" of the members of the claimed genera of survivin and HDLC1 variants but Appellants have pointed to no disclosure of *structural* attributes or features that are possessed by members of the claimed genera and distinguish them from, among other things, polypeptides that are at least 80% similar to survivin or HDLC1 but that do not interact with the other protein.

With regard to Example 14, even though the Written Description Examination Guidelines and the accompanying Training Materials can be helpful in understanding how to apply the relevant case law (at least at the time the Guidelines were adopted in 2001), they do not create any per se rules or rigid tests. For the reasons discussed above, we conclude that the Examiner has correctly applied the written description requirement of 35 U.S.C. § 112, first paragraph, to the facts of this case.

SUMMARY

We reverse the rejection for lack of enablement but we affirm the rejection of claims 40-50 for lack of adequate written description and the rejection of claims 43, 49, and 50 for including new matter.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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